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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,953	06/25/2003	William G. Bornmann	D6371D	3108

7590 03/19/2004

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EXAMINER	
SHIAO, REI TSANG	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,953	BORNMANN ET AL.	
	Examiner	Art Unit	
	Robert Shiao	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *application filed on 06/25, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the provisional applications: 60/277,116 with a filing date 03/19/2001.

2. Claims 1-21 are pending in the application.

Election/Restriction

3. The Markush group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. For these reasons provided below, restriction to one of the following Groups is required under 35 U.S.C. 121, wherein an Group is a set of patentably distinct inventions of a broad statutory category (e.g. Compounds, Methods of Use, Methods of Making, etc.):

I. Claims 1-16, in part, drawn to compounds/compositions of formula (I), wherein the variable R^1 represents $NHCH_2Ph$, $NHCH_3$, $NHCH_2CH_3$, $N(CH3)_2$, $N(CH_2CH_3)_2$, $NHCH_2(2,4\text{-}(OCH_3)_2Ph$, $NHCH_2(4\text{-}NO_2\ Ph)$, hexamethyleneamine, methyl 2- or 3 - hexamethy1eneamine carboxy1ate, or hepamethy1eneamine thereof; variables R^2, R^3, and R^4 are as defined in claim 1;

and their processes of making and methods of use, classified in classes 514/544/546, numerous subclasses. If this group is elected, applicants are requested to elect a single species for the search purpose.

II. Claims 1-16, in part, drawn to compounds/compositions of formula (I), wherein the variable R^1 represents pyrrole, indole, indoline, or imidazole thereof; variables R^2, R^3, and R^4 are as defined in claim 1; and their processes of making and methods of use, classified in classes 514/548, numerous subclasses. If this group is elected, applicants are requested to elect a single species for the search purpose.

III. Claims 1-16, in part, drawn to compounds/compositions of formula (I), wherein the variable R^1 represents proline, azetidine, or aziridine thereof; variables R^2, R^3, and R^4 are as defined in claim 1; and their processes of making and methods of use, classified in classes 514/548, numerous subclasses. If this group is elected, applicants are requested to elect a single species for the search purpose.

IV. Claims 1-16, in part, drawn to compounds/compositions of formula (I), wherein the variable R^1 represents 1,4-dioxan-2-yl-methylamine, 3,4-dihydro-2H-1, 4-benzoxazin-6-ol, 6-methoxy- 1,2,3,4-tetrahydro-isoquinoline, or piperazin-1-yl-pyridin-l-3-yl- methanone thereof; variables R^2, R^3, and R^4 are as defined in

claim 1; and their processes of making and methods of use, classified in classes 514/544/546, numerous subclasses. If this group is elected, applicants are requested to elect a single species for the search purpose.

V. Claims 1-16, in part, drawn to compounds/compositions of formula (I), receiving compounds not encompassed in Groups I-IV, and their processes of making and methods of use, classified in classes 514/544/546/548, numerous subclasses. If this group is elected, applicants are requested to elect a single species for the search purpose.

VI. Claims 17-19, drawn to methods of use (i.e., treating neoplastic diseases) of the compound (S,S,R)-(-)-actinonin, classified in classes 514, numerous subclasses.

VII. Claims 20-21, drawn to methods of use (i.e., inhibition of the growth of tumor cells) of the compound (S,S,R)-(-)-actinonin, classified in classes 514, numerous subclasses.

If Group VI-VII is elected, then election of one of the following methods of use is required:

A. Method of treating human ovarian carcinoma

B. Method of treating prostate carcinoma

C. Method of treating ovarian cancer cells

D. Method of treating prostate cancer cells

In accordance with the decisions in ***In re Harnisch***, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and ***Ex parte Hozumi***, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 U.S.C. 103.

Where an election of any one of Groups I-VII is made, an election of a single species is further required including an exact definition of each substitution on the base molecule (i.e., the formula of claim 1), wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has substituent groups R^1 or R^2, wherein R^1 and R^2 are independently recited to be any one of $N(CH3)_2$, $N(CH_2CH_3)_2$, methyl, etc., then applicant must select a single substituent of R^2, for example methyl, and each subsequent variable position.

Should applicant traverse on the ground that the compounds are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable

over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventors must be amended in compliance with 37C.F.R. 1.48(b) if one of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37CFR 1.17(i).

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can **set forth** a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

Rationale Establishing Patentable Distinctiveness Within Each Group

Each Invention Set listed above is directed to or involves the use or making of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over either of the other inventions, i.e. they are patentable over each other. Chemical structures which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holdings of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:

Each of Groups I-VI are distinct and independent, one from the other on the basis of structure defined in the claimed compounds as directed to a compound of formula of claim 1 having various heteroaryl or heterocycle moieties (i.e., thiazole,

thiadiazole, oxazole, pyridine, piperazine, thiophene, etc). Absent factual evidence to the contrary, each is a different chemical compound.

Each of different methods of use inventions set forth in Groups VI-VII is unrelated. Invention are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). Methods of use are unrelated if one of three difference are found between them. These are 1) the population being treated, 2) the material being used, and 3) the methodology for treatment. If any one or more of this difference exist and are patently distinct, then the methods are unrelated. In the instant case, the different methods of use inventions are unrelated because patient population treated for each method is divergent. For example, a method of treating human ovarian carcinoma presumes that the patients being treated have ovarian carcinoma, while a method of inhibiting the growth of tumor cells presumes that the subject being treated is tumor cells.

Groups I-V and VI-VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (MPEP 806.05(h)). In the instant case, the actinonin compounds as claimed can be used in a materially different process of using, i.e., treating autoimmune disease, see CAS: 136:215000. The instant actinonin compounds

are as demonstrated throughout the specification and in claims 1-21 which are directed to several different methods of use, for example treating human neoplastic diseases.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

In addition, because of the plethora of classes and subclasses in each of the Groups, a serious burden is imposed on the examiner to perform a complete search of the defined areas. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

for Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626

Robert Shiao, Ph.D.
Patent Examiner
Art Unit 1626

March 17, 2004